STN-Structure Search 6-1-06

10/530,664

=> d ibib abs hitstr 1-22

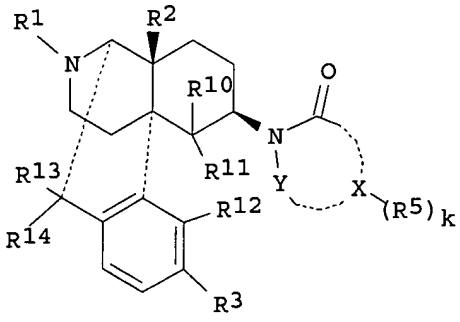
L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:437549 CAPLUS
TITLE: Analgesic
INVENTOR(S): Izumimoto, Naoki; Kawamura, Kuniaki; Komagata, Toshikazu; Hashimoto, Tadatoshi; Nagabukuro, Hiroshi
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006049248	A1	20060511	WO 2005-JP20297	20051104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-320583 A 20041104
GI



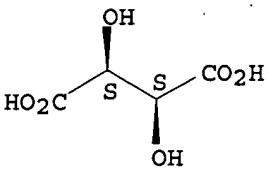
I

AB An analgesic widely applicable to various pains induced by various causes. The analgesic contains as an active ingredient either a specific morphinan derivative having a nitrogenous cyclic substituent in the 6-position such as compound (I), or a pharmacol. acceptable acid addition salt thereof.

IT **681030-14-8P 681030-15-9P 681030-28-4P 681030-75-1P 681031-03-8P 885322-11-2P 885322-12-3P 885322-13-4P 885322-15-6P 885322-17-8P 885322-18-9P 885322-19-0P 885322-20-3P 885322-21-4P 885322-22-5P 885322-23-6P 885322-26-9P 885322-29-2P 885322-31-6P 885322-33-8P 885322-36-1P 885322-38-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

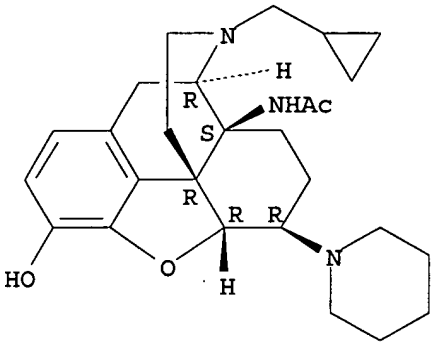
L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:273663 CAPLUS
DOCUMENT NUMBER: 144:312240
TITLE: Preparation of substituted epoxymorphinans as opioid receptor modulators
INVENTOR(S): Dolle, Roland E.; Le Bourdonnec, Bertrand; Sutton, Jonathan Mark; Eastwood, Paul; Warner, Ines
PATENT ASSIGNEE(S): Adolor Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 88 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006063792	A1	20060323	US 2005-227685	20050915
WO 2006034039	A2	20060330	WO 2005-US33179	20050916

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

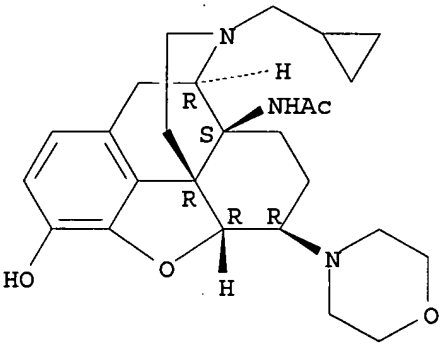
PRIORITY APPLN. INFO.: US 2004-610721P P 20040917
US 2005-227685 A 20050915

GI



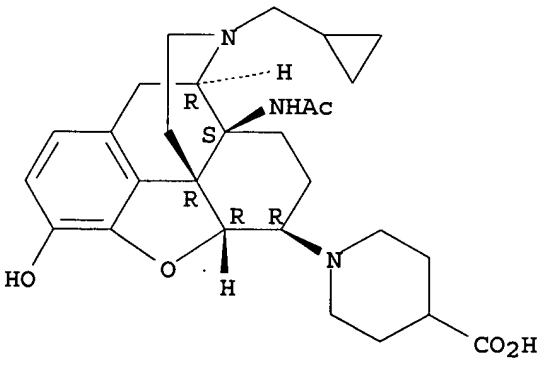
RN 879875-16-8 CAPLUS
CN Acetamide, N-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxy-6-(4-morpholinyl)morphinan-14-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



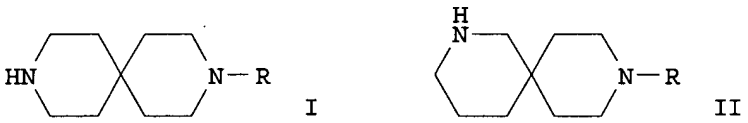
RN 879875-30-6 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[(5α,6β)-14-(acetylamino)-17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1235384 CAPLUS
DOCUMENT NUMBER: 144:128934
TITLE: Annulation of Primary Amines to Piperazines and Diazaspirocycles Utilizing α-Methyl Benzyl Resin

AUTHOR(S): Macleod, Calum; Martinez-Teipel, Blanca I.; Barker, William M.; Dolle, Roland E.
CORPORATE SOURCE: Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SOURCE: Journal of Combinatorial Chemistry (2006), 8(1), 132-140
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:128934
GI

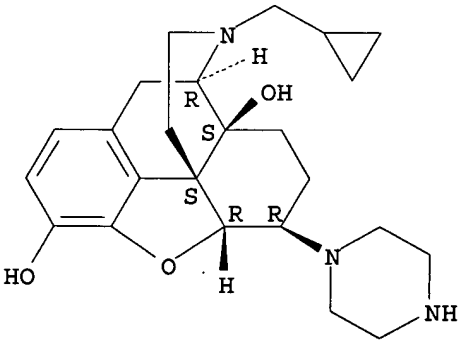


AB The microwave-assisted solid-phase synthesis of 1-R-piperazines (R = Ph2CHCH2, 3-FC6H4CH2, cyclopentyl, 2-thienylmethyl, etc.), 3,9-diazaspiro[5.5]undecanes I and 2,9-diazaspiro[5.5]undecanes II is reported. The synthesis relies on the direct annulation of primary amines RNH2 with resin-bound bismesylates, e.g. XCHMeOCON(CH2CH2OSO2Me)2 (X = resin) for synthesis of piperazines. Critical to the success of this chemical was the development of α-Me benzyl carbamate resin linker. This resin permits the cleavage of the heterocycles under mildly acidic conditions, free of contaminating linker-derived N-alkylated byproducts.
IT **873433-28-4P 873433-70-6P 873434-10-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of functionalized piperazines and diazaspiroundecanes via heterocyclization of primary amines with resin-bound bis(mesylates) under microwave irradiation conditions)
RN 873433-28-4 CAPLUS
CN Morphinan-3,14-diol, 17-(cyclopropylmethyl)-4,5-epoxy-6-(1-piperazinyl)-, (5α,6β)-, tris(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

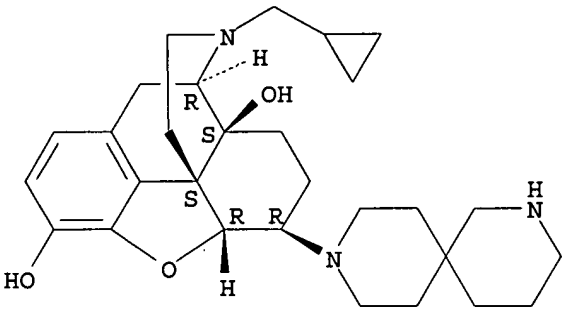
CM 1

CRN 873433-27-3
CMF C24 H33 N3 O3

Absolute stereochemistry.

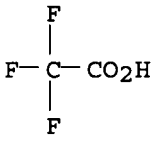


CM 2



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1103579 CAPLUS
DOCUMENT NUMBER: 143:379869
TITLE: Morphinan derivatives as anti-itching agents
INVENTOR(S): Izumimoto, Naoki; Komagata, Toshikazu; Honda, Toshiyuki; Kawai, Koji
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005094826	A1	20051013	WO 2005-JP6015	20050330

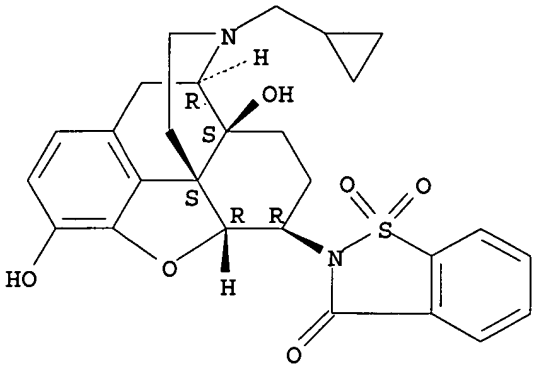
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-97798 A 20040330
OTHER SOURCE(S): MARPAT 143:379869

AB Disclosed is a novel anti-itching agent useful for the treatment of itching accompanied by various diseases. The anti-itching agent contains

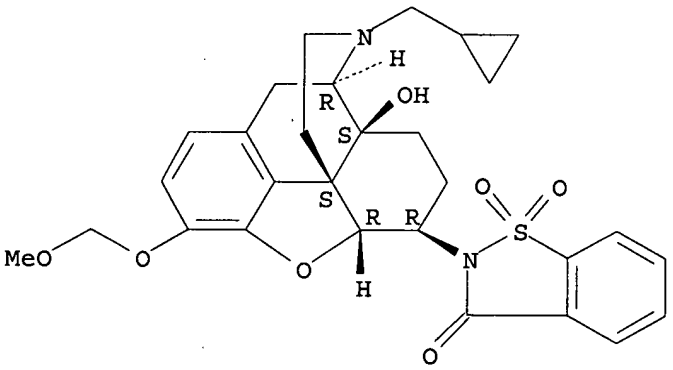
NAME)

Absolute stereochemistry.



RN 866572-72-7 CAPLUS
CN 1,2-Benzisothiazol-3(2H)-one, 2-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-14-hydroxy-3-(methoxymethoxy)morphinan-6-yl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

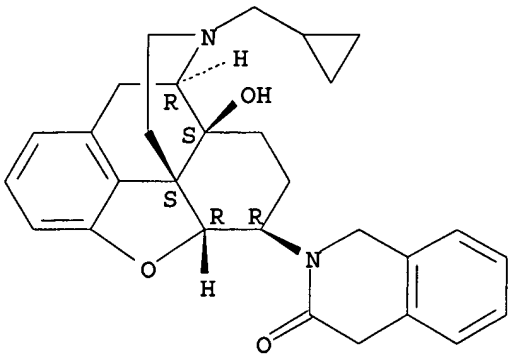


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1056264 CAPLUS
DOCUMENT NUMBER: 143:477783
TITLE: Solid/solution-phase annulation reagents: Single-step synthesis of cyclic amine derivatives
AUTHOR(S): Dolle, Roland E.; MacLeod, Calum; Martinez-Teipel, Blanca; Barker, William; Seida, Pamela R.; Herbertz, Torsten
CORPORATE SOURCE: Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SOURCE: Angewandte Chemie, International Edition (2005), 44(36), 5830-5833
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:477783
GI

(cyclopropylmethyl)-4,5-epoxy-14-hydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

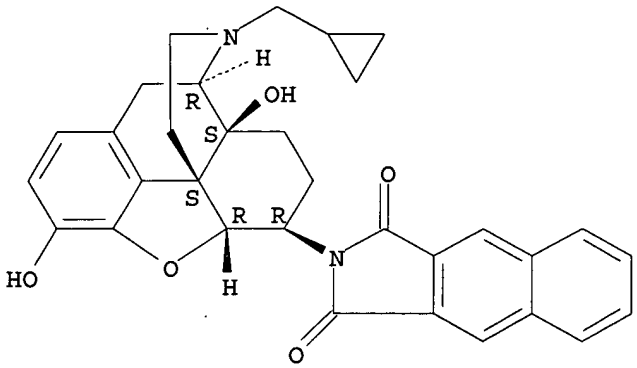
Inventor

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:333718 CAPLUS
DOCUMENT NUMBER: 140:339518
TITLE: Preparation of morphinan derivatives having nitrogen-containing heterocyclic group as remedies or prophylactic agents for urinary frequency or urinary incontinence
INVENTOR(S): Izumimoto, Naoki; Kawai, Koji; Kawamura, Kuniaki; Fujimura, Morihiro; Komagata, Toshikazu
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033457	A1	20040422	WO 2003-JP12890	20031008
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501389	AA	20040422	CA 2003-2501389	20031008
AU 2003272944	A1	20040504	AU 2003-272944	20031008
EP 1555266	A1	20050720	EP 2003-754030	20031008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014754	A	20050726	BR 2003-14754	20031008
US 2006040970	A1	20060223	US 2005-530664	20050406
NO 2005002167	A	20050616	NO 2005-2167	20050503
PRIORITY APPLN. INFO.:			JP 2002-295616 A	20021009
			WO 2003-JP12890 W	20031008

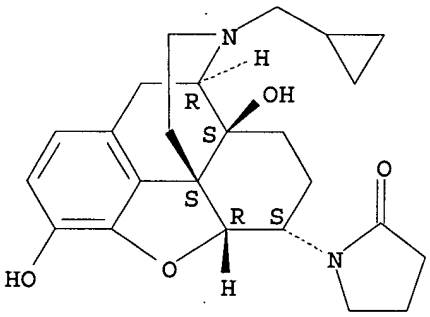
CN 1H-Benz[f]isoindole-1,3(2H)-dione, 2-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



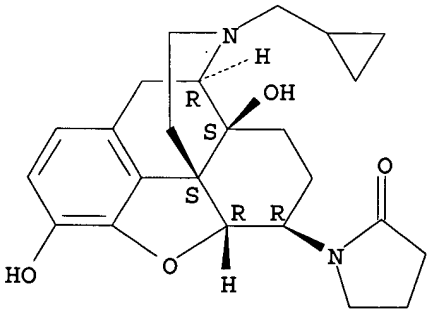
RN 681033-25-0 CAPLUS
CN 2-Pyrrolidinone, 1-[(5α,6α)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681033-27-2 CAPLUS
CN 2-Pyrrolidinone, 1-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

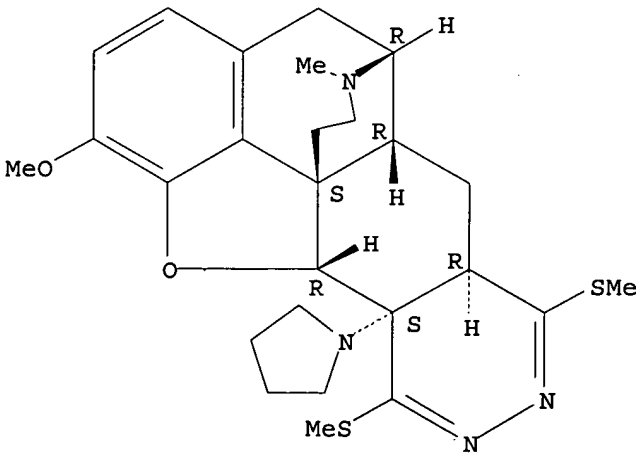


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:687571 CAPLUS
DOCUMENT NUMBER: 127:346547
TITLE: Synthesis of novel pyridazinomorphinans by inverse-electron-demand cycloaddition and their binding to μ- and κ-receptors
AUTHOR(S): Klindert, Thilo; Stroetmann, Isabel; Seitz, Gunther; Hofner, Georg; Wanner, Klaus T.; Frenzen, Gerlinde; Eckhoff, Brigitta
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut, Universitat Marburg, Marburg, D-35032, Germany
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1997), 330(6), 163-168
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of novel pyridazinomorphinans were synthesized by the inverse-electron-demand Diels-Alder reaction of 3,6-disubstituted 1,2,4,5-tetrazines with enamines derived from dihydrocodeinone and with codeinone. Reduction of some of the pyridazinomorphinans did not furnish the expected pyrroloepoxymorphinans. In all cases, investigated reductive cleavage of the epoxy bridge was observed to yield dihydropyridazino- or pyrrolomorphinans. The structures of all new compds. were assigned by the spectral data, that of the cycloadduct of codeinone was addnl. verified by x-ray crystallog. Some of the compds. were evaluated for their affinity at μ- and κ-opioid receptors in radioligand binding assays. Their ability to inhibit [3H]DAMGO binding at μ and [H]U 69.593 binding at κ receptors, resp., as compared to codeine is lower.
IT **198136-91-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridazinomorphinans by inverse-electron-demand cycloaddn. and binding to μ- and κ-receptors)
RN 198136-91-3 CAPLUS
CN 4,8-Methano-5H-benzofuro[2,3-f]pyrido[4,3-g]phthalazine, 6,7,8,8a,9,9a,13a,13b-octahydro-1-methoxy-7-methyl-10,13-bis(methylthio)-13a-(1-pyrrolidinyl)-, [8R-(4bS*,8α,8aβ,9aα,13aα,13bβ)]- (9CI) (CA INDEX NAME)

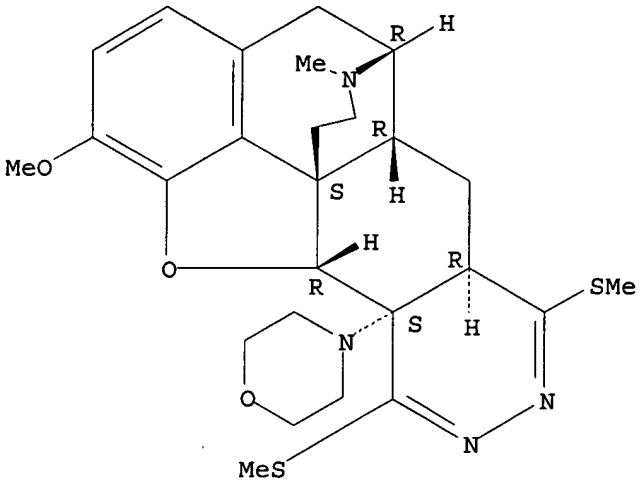
Absolute stereochemistry.



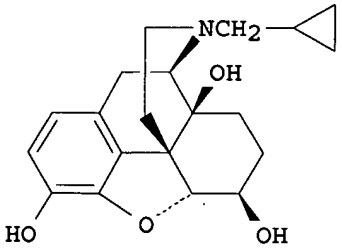
IT **198136-92-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridazinomorphinans by inverse-electron-demand cycloaddn.

and binding to μ- and κ-receptors)
RN 198136-92-4 CAPLUS
CN 4,8-Methano-5H-benzofuro[2,3-f]pyrido[4,3-g]phthalazine, 6,7,8,8a,9,9a,13a,13b-octahydro-1-methoxy-7-methyl-10,13-bis(methylthio)-13a-(4-morpholinyl)-, [8R-(4bS*,8α,8aβ,9aα,13aα,13b β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:213594 CAPLUS
DOCUMENT NUMBER: 122:81697
TITLE: Stereoselective synthesis of β-naltrexol, β-naloxol, β-naloxamine, β-naltrexamine and related compounds by the application of the Mitsunobu reaction
AUTHOR(S): Simon, Csaba; Hosztafi, Sandor; Makleit, Sandor
CORPORATE SOURCE: Alkaloida Chem. Company Ltd., Tiszavasvari, H-4440, Hung.
SOURCE: Tetrahedron (1994), 50(32), 9757-68
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:81697
GI



I

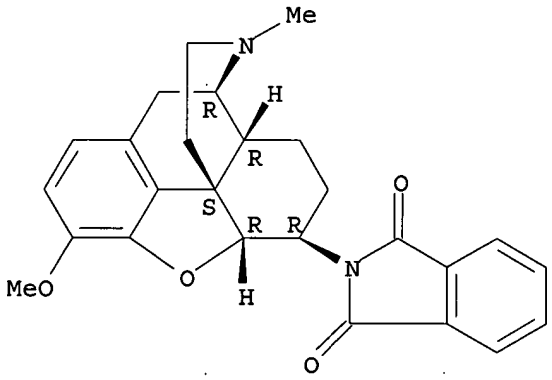
AB As a continuation of our work, aimed at adopting the Mitsunobu reaction in the morphine series, a few representatives of dihydroisocodeines and dihydroisomorphines and their 14β-hydroxy analogs, e.g. I, were

prepared P-Nitrobenzoic acid was used as carboxylic acid and the prepared esters were cleaved to obtain the title compds. Using phthalimide as acidic component several new 6β-phthalimidodihydromorphine and dihydrocodeine derivs. and their 14β-hydroxy analogs have been synthesized. Cleavage of the phthalimido derivs. with hydrazine hydrate afforded the corresponding 6β-amino derivs.

IT **142729-59-7P 142729-60-0P 160359-48-8P**
160359-49-9P 160359-50-2P 160359-51-3P
160359-52-4P 160359-53-5P 160359-54-6P
160359-55-7P 160359-56-8P 160359-57-9P
160359-58-0P 160359-59-1P 160359-60-4P
160359-61-5P 160359-62-6P 160359-63-7P
160359-64-8P 160359-65-9P 160359-66-0P
160359-67-1P 160359-68-2P 161273-21-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective synthesis of naltrexol, naloxol, naloxamine, naltrexamine and related compds. by the application of the Mitsunobu reaction)

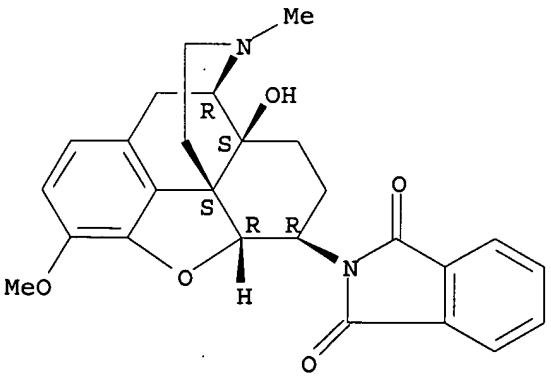
RN 142729-59-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[(5α,6β)-4,5-epoxy-3-methoxy-17-methylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142729-60-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[(5α,6β)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

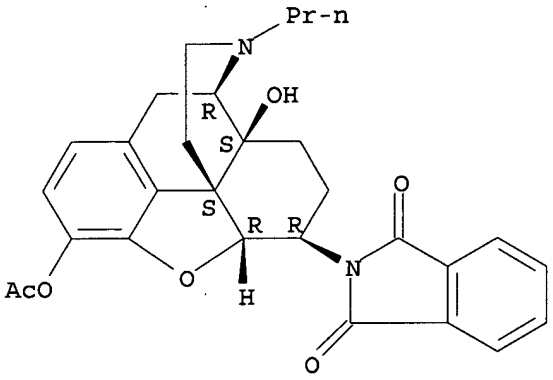
Absolute stereochemistry.



RN 160359-48-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[(5α,6β)-4,5-epoxy-3-methoxy-17-

CN 1H-Isoindole-1,3(2H)-dione, 2-[(5α,6β)-3-(acetyloxy)-4,5-epoxy-14-hydroxy-17-propylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

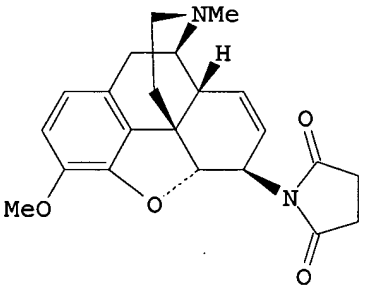
Absolute stereochemistry.



L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1992:490553 CAPLUS
DOCUMENT NUMBER:	117:90553
TITLE:	Substituent-dependent conformational changes in 6β-substituted codeine derivatives
AUTHOR(S):	Szilagyi, Laszlo; Makleit, Sandor; Hosztafi, Sandor; Simon, Csaba
CORPORATE SOURCE:	Dep. Org. Chem., L. Kossuth Univ., Debrecen, H-4010, Hung.
SOURCE:	Magnetic Resonance in Chemistry (1992), 30(6), 552-7 CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE:	Journal
LANGUAGE:	English

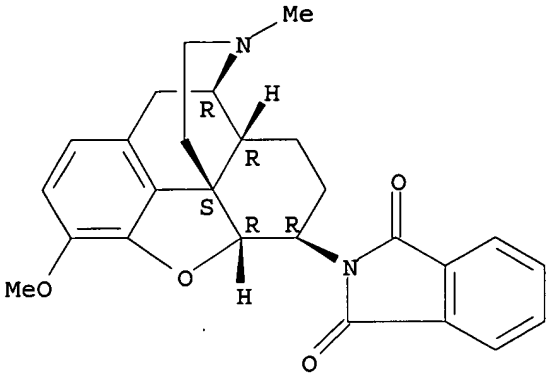
GI



I

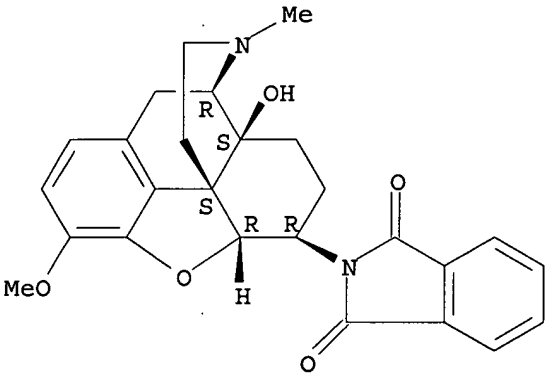
AB Complete 1H and 13C NMR data are reported for eleven isocodeine derivs., e.g. I, and seven dihydroisocodeine derivs. bearing various substituents at position 6. In isocodeines having bulky succinimido or phthalimido groups at C-6 rings C adopts a half-boat conformation, characterized by the quasi-equatorial orientation of the C-6-N bond. The distortion from the usual boat form is due to steric interactions between C-14 and β-substituents at C-6, and it is greater in 14-hydroxy derivs. than in isocodeines unsubstituted at this position. In dihydroisocodeines the conformation of ring C is close to a chair, irresp. of the steric demand of the substituent at C-6.

IT **141844-27-1 142729-58-6 142729-59-7 142729-60-0**
RL: PRP (Properties)

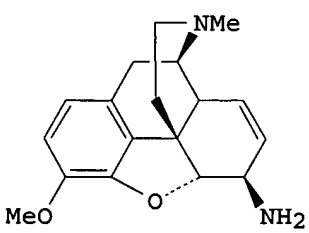


RN 142729-60-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[(5α,6β)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

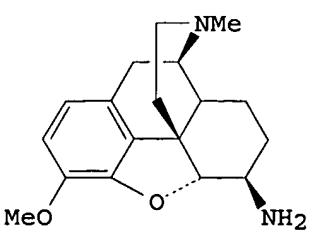
Absolute stereochemistry.



L4 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:426891 CAPLUS
DOCUMENT NUMBER: 117:26891
TITLE: Application of the Mitsunobu reaction for morphine compounds. Preparation of 6β-aminomorphine and codeine derivatives
AUTHOR(S): Simon, Csaba; Hosztafi, Sandor; Makleit, Sandor
CORPORATE SOURCE: Alkaloida Chem. Fact., Tiszavasvari, H-4400, Hung.
SOURCE: Synthetic Communications (1992), 22(6), 913-21
CODEN: SYNCAV; ISSN: 0039-7911
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:26891
GI



I



II

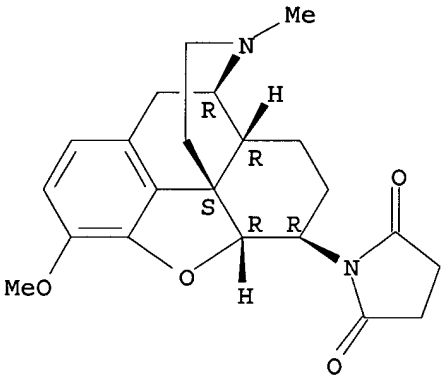
AB By the application of the Mitsunobu reaction several new 6β-aminomorphine and codeine derivs., carrying a Δ7,8 double bond in ring C, e.g. I, were synthesized. The catalytic hydrogenation of these compds. offered a new stereoselective way for the synthesis of the corresponding 6β-amino-dihydro analogs, e.g. II. The different conformation of ring C of the saturated and unsatd. amino compds. allows to study the structure-activity relationship, and by tritiation of the unsatd. derivs. the substrate-receptor interactions can be examined

IT **141844-27-1P 141844-28-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 141844-27-1 CAPLUS

CN 2,5-Pyrrolidinedione, 1-[(5α,6β)-4,5-epoxy-3-methoxy-17-methylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

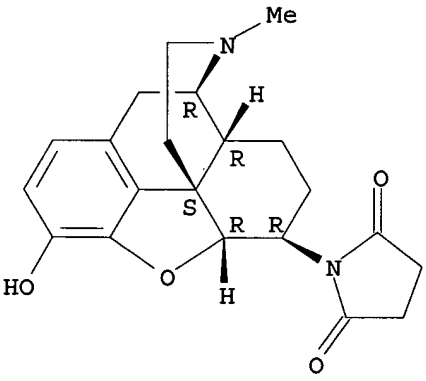
Absolute stereochemistry.



RN 141844-28-2 CAPLUS

CN 2,5-Pyrrolidinedione, 1-[(5α,6β)-4,5-epoxy-3-hydroxy-17-methylmorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:522568 CAPLUS

DOCUMENT NUMBER: 101:122568

TITLE: Design and synthesis of naltrexone-derived affinity labels with nonequilibrium opioid agonist and

antagonist activities. Evidence for the existence of different μ receptor subtypes in different tissues

AUTHOR(S): Sayre, L. M.; Larson, D. L.; Takemori, A. E.; Portoghese, P. S.

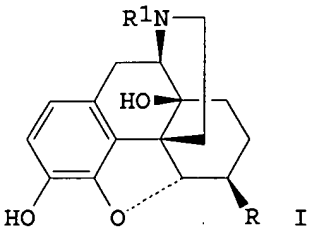
CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Journal of Medicinal Chemistry (1984), 27(10), 1325-35
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

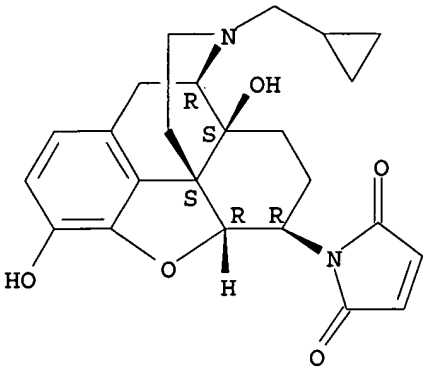
AB β-Funaltrexamine (β-FNA) analogs I (R = NHCOCH:CHCO2Me, NHCOC.tplbond.CH, NHCOCH2HgCl, etc.; R1 = CH2CH:CH2 or CH2CH(CH2)2) were prepared and evaluated for opioid agonist and antagonist activities in guinea pig ileum (GPI) and mouse vas deferens (MVD) in vitro assays. Several I behaved like β-FNA showing reversible agonist activity at κ-opioid receptors and irreversible antagonist activity at μ-opioid receptors. 17-(Cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxy-6β-(maleimidoacetimido)morphinan (I; R = maleimidoacetimido; R1 = CH2CH(CH2)2) [91409-44-8] behaved very differntly from β-FNA exhibiting considerably greater μ-receptor antagonism in the MVD relative to the GPI; this suggests that different proportions of μ-receptor subtypes exist in the 2 tissues. Several of the agents tested, including some nonreactive control compds. (I; R = NHCOPh or NHCO(CH2)2CO2Me; R1 = CH2CH(CH2)2) displayed an unusual type of persistant κ-agonist activity in the GPI; this activity was reversibly antagonized by naloxone. Receptor models are presented to explain this effect. A few of the reactive ligands displayed a true nonreversible κ-agonist activity, suggesting a covalent association with the receptor; of note in this regard was 17-(cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxy-6β-propiolamidomorphinan (I; R = NHCOC.tplbond.H; R1 = CH2CH(CH2)2) [91409-41-5] which appeared to be an irreversible mixed agonist-antagonist at κ- and μ-receptors. Structure-activity relations are discussed.

IT **91409-42-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and opiate receptor agonist-antagonist activity of)

RN 91409-42-6 CAPLUS

CN 1H-Pyrrole-2,5-dione, 1-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:482295 CAPLUS
DOCUMENT NUMBER: 67:82295
TITLE: Endoetheno-codeines and -morphines
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: Neth. Appl., 42 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6610236		19670123	NL 1966-10236	19660720
US 3318884		19670509	US 1965-511345	19651203
US 3318885		19670509	US 1965-511344	19651203
US 3318886		19670509	US 1965-511365	19651203
PRIORITY APPLN. INFO.:			US	19650721
			US	19651203

GI For diagram(s), see printed CA Issue.

AB The preparation of the title compds. (I) is given. Thus, 4 ml. pyrrolidine is added slowly to a suspension of 4 g. codeinone in 40 ml. hot MeOH in a N atmospheric After cooling the mixture is kept 1-2 hrs. at 0-5° to yield 3.5 g. of the methanolate (IIa), m. 112-14°, of II (R1 = R2 = Me). On refluxing a solution of 245 mg. IIa in 25 ml. anhydrous C6H6 for 4 hrs. 112 mg. III (R1 = R2 = Me) (IIIa), m. 117-20° (n-hexane), is obtained. Both reaction of IIa and of IIIa with a suitable dienophile of formula CH2:CHR3 yields I. The assignment of the endo structure α and of the exo structure β to the resulting epimers and to those of other I is based on N.M.R. spectra. Thus, a mixture of 200 mg. IIa and 5 ml. CH2:CHCN is refluxed 2 hrs. and evaporated to yield 125 mg. of a mixture of epimers of I (R1 = R2 = Me, R3 = CN) (Ia), m. 197-200° (decomposition) (Me2-CO-n-hexane). This mixture is resolved by partition chromatog. to yield α-Ia, m. 201-2° (decomposition), and β-Ia, m. 205-7° (decomposition). The following I (R1 = R2 = Me, R3 and m.p. given) are similarly prepared: α-CHO (Ib), 165-7°; α-CO2Et (Ic), 219-21° (decomposition); α + β-PhCO (Id), 182-3° (decomposition); α + β-Ac (Ie), -. Refluxing a mixture of 80 mg. IIIa and 5 ml. CH2:CHCN for 2 hrs. yields 64 mg. (α + β)-Ia, m. 195-9° (decomposition) (Me2CO-hexane). In a similar manner are prepared: α-Ib, m. 165-7°, and α-Ie, m. 104-7°. α-Ic (1 g.) is added to a suspension of 1 g. LiAlH4 in 100 ml. Et2O. After stirring the mixture 2 hrs. at room temperature, it is treated with saturated aqueous K Na tartrate. Working up of the organic solution yields

646 mg. crude I (R1 = R2 = Me, R3 = CH2OH) (If), m. 150-7°, which on recrystn. yields α-If, m. 162-5° (MeOH). The same product (m. 148-52°) is obtained by reduction of α-Ib with NaBH4 in EtOH. Reduction of 500 mg. (α + β)-Id with 500 mg. LiAlH4 in 50 ml. Et2O gives 238 mg. (α + β)-I (R1 = R2 = Me, R3 = CH(OH)Ph) (Ig), m. 195-9° (MeOH). Further, 500 mg. metallic Li is added portionwise to a mixture of 500 mg. (α + β)-Id, 50 ml. Et2O, and 12.5 ml. MeI. After stirring the mixture of 30 min. it is decomposed to yield 231 mg. crude I [R1 = R2 = Me, R3 = CMe(OH)Ph] (Ih), m. 143-6°, which is purified by partition chromatog. to yield α-Ih, m. 150-2°. Similarly prepared are the following I (R1 = R2 = Me, R3 and m.p. given): (α + β)-CMe(OH)Pr (Ii), -; (α + β)-CMe2OH (Ij), m. 184-6°; (α + β)-CH(OH)Me (Ik), m. 170-4°. Treatment of 1 mole Ic with 2 moles MeLi also yields α-Ij, m. 190-2°. A mixture of 100 mg. BrCN, 200 mg. α-Ij, and 5 ml. CHCl3 is refluxed 24 hrs. to yield 100 mg. I (R1 = Me, R2 = CN, R3 = α-CMe2OH) (Il), m. 216-17° (Me2CO-hexane). Similarly prepared is I (R1 = Me, R2 = CNx, R3 = Ac) (Im). A mixture of 2.36 g. Il, 2.36 g. KOH, and 24 ml. ethylene glycol is heated 30 min. at 170°. After cooling, the mixture is diluted with H2O and extracted with CH2Cl2 to yield 1.5 g.

I (R1 = Me, R2 = H, R3 = α-CMe2OH) (In). Cyclopropanecarbonyl chloride (1.54 g.) is added to a stirred mixture of 1.5 g. K2CO3, 1.5 g. In, and 35 ml. Et2O. After stirring the suspension for 2 hrs. it is worked up to yield 861 mg. I (R1 = Me, R2 = cyclopropylcarbonyl, R3 = α-CMe2OH (Io), m. 211-14° [Me2CO-hexane). A mixture of 125 mg. LiAlH4, 250 mg. Io, and 10 ml. anhydrous tetrahydrofuran is refluxed 1 hr. After cooling a saturated aqueous solution of K Na tartrate is added and the organic layer worked up as usual to yield 203 mg. I (R1 = Me, R2 = cyclopropylmethyl, R3 = α-CMe2OH) (Ip), m. 152-3° (MeOH-H2O). A mixture of 100 mg. α-Ij, 400 mg. KOH, and 2 ml. ethylene glycol is heated 1 hr. at 210-15° to yield 30 mg. I (R1 = H, R2 = Me, R3 = α-CMe2OH) (Iq), m. 273-4° (Me2CO-hexane). Similar saponification of Ip yields I (R1 = H, R2 = cyclopropylmethyl, R3 = α-CMe2OH) (Ir). Finally a solution of 392 mg. If in 1.6 ml. Ac2O and 1.6 ml. C5H5N is heated 1 hr. at 100° to yield 213 mg. I (R1 = R2 = Me, R3 = (α + β)-CH2OAc) (Is), m. 147-9° (Me2CO-hexane). The compds. are analgesics and (or) antagonists of analgesics. Some of them, in particular Ia, Id, If, Ii, Ij, and Iq, are narcotics with morphine-like analgesic activity. Ir is an antagonist of morphine and can be used both as antidote in case of morphine poisoning and as a non-addicting analgesic. A 3rd group, especially Ib, Ih, In, and Is, although lacking antagonistic activity, still can be used as nonnarcotic analgesics. In some cases the latter compds. also have antiinflammatory activity. The various indicated properties are established by standard pharmacol. methods. The compds. are applied in the usual pharmaceutical formulations.

IT **16251-66-4P 16276-86-1P 16276-87-2P**
16276-88-3P 16276-89-4P 16276-92-9P
16276-93-0P 16276-94-1P 16276-96-3P
16276-97-4P 16276-98-5P 16276-99-6P
16277-00-2P 16333-36-1P 16333-37-2P
16427-96-6P 17097-36-8P 17097-37-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

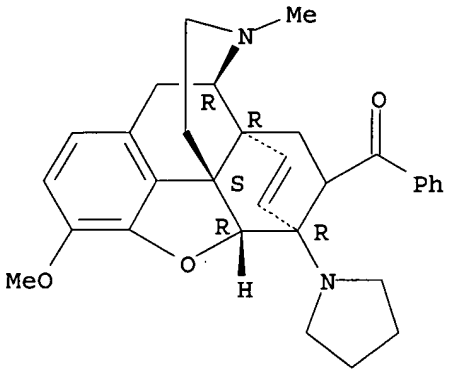
RN 16251-66-4 CAPLUS

CN 6,14-endo-Ethenocodeine, 7α-cyano-6-deoxy-7,8-dihydro-6-(1-pyrrolidinyl)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

IT **16276-90-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoisomers)
RN 16276-90-7 CAPLUS
CN 6,14-endo-Ethenocodeine, 7-benzoyl-6-deoxy-7,8-dihydro-6-(1-pyrrolidinyl)-(8CI) (CA INDEX NAME)

Absolute stereochemistry.

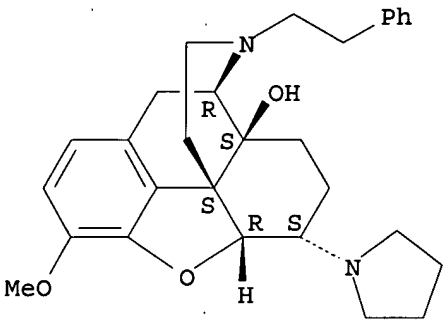


L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:18789 CAPLUS
DOCUMENT NUMBER: 66:18789
TITLE: 14-Hydroxy-6α-aminodihydrocorsides
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku
PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 5 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41018826	B4	19641031	JP	19640203

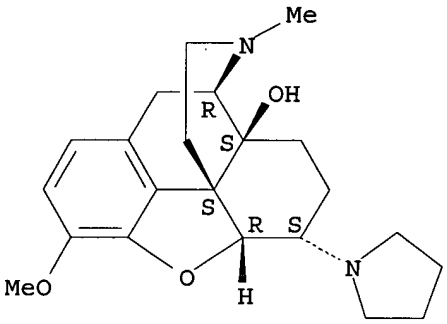
GI For diagram(s), see printed CA Issue.
AB I is treated with amine and the resulting II is subjected to catalytic reduction to give III, useful as an analgesic and antiphlogistic. Ts is tosyl in this abstract In an example, 4.7 g. I (R = Me) is boiled 40 hrs. in 200 cc. C6H6 with 20 cc. pyrrolidine, the mixture cooled and extracted with dilute HCl, and the extract washed with C6H6, made alkaline with 30% KOH under ice-cooling, and extracted with C6H6 to give 2.9 g. II (R = Me, Z = 1-pyrrolidinyl), m. 105-9°. II (3.7 g.) is dissolved in 50 cc. 10% AcOH, shaken in a H stream with 2 g. 10% Pd-C 2.5 hrs., filtered, and the filtrate made alkaline with 30% KOH and extracted with C6H6 to give 1.7 g. III (R = Me, Z = 1-pyrrolidinyl), m. 193-5°. Similarly prepared are the following III (R, Z, and m.p. given): Me, piperidino, 170-3°; Me, NMe2, 115-16°; phenethyl, 1-pyrrolidinyl, 91-3°.
IT **14978-25-7P 15012-13-2P 15012-14-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 14978-25-7 CAPLUS
CN Morphinan-14-ol, 4,5α-epoxy-3-methoxy-17-phenethyl-6α-(1-pyrrolidinyl)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



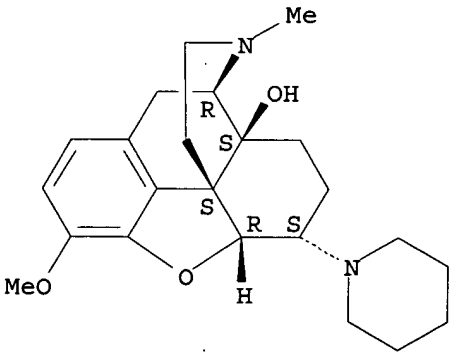
RN 15012-13-2 CAPLUS
CN Morphinan-14-ol, 4,5α-epoxy-3-methoxy-17-methyl-6α-(1-pyrrolidinyl)-, stereoisomer (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 15012-14-3 CAPLUS
CN Morphinan-14-ol, 4,5α-epoxy-3-methoxy-17-methyl-6α-piperidino- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:18787 CAPLUS
DOCUMENT NUMBER: 66:18787
TITLE: 6-Aminodihydromorphides
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku

10/530,664

PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 4 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41018824	B4	19641031	JP	19640203

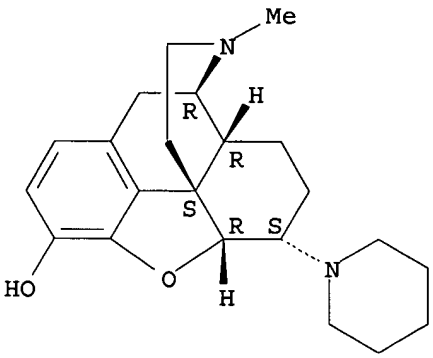
GI For diagram(s), see printed CA Issue.

AB Manufacture of I, useful as analgesic and antiphlogistic, by demethylation of II is described. In an example, 0.01 mole II (Z = α-1-pyrrolidinyl, R1 = H, R2 = Me) is heated in a N stream with a mixture of 15 cc. pyridine and 50 cc. 25% ethanolic HCl, 50 cc. warm H2O added, and the mixture adjusted to pH 5.0 with 30% KOH, washed with CHCl3, adjusted to pH 13.0 with 30% KOH, washed with CHCl3, adjusted to pH 9.0 with NH4Cl, and extracted with CHCl3 to give I [Z = α-(1-pyrrolidinyl), R1 = H, R2 = Me], m. 130-5°. Similarly prepared are the following I (Z, R1, R2, and m.p. given): β-piperidino, H, Me, 216.5-17.5° (AcOEt); α-(1-pyrrolidinyl), OH, Me, 254-6° (CHCl3-EtOH); α-piperidino, H, Me, 213-16° (AcOEt); α-(1-pyrrodiidinyl), OH, phenethyl, 238-42° (decomposition); α-NMe2, OH, Me, 261-4°.

IT **13851-14-4P 13851-15-5P 14912-47-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

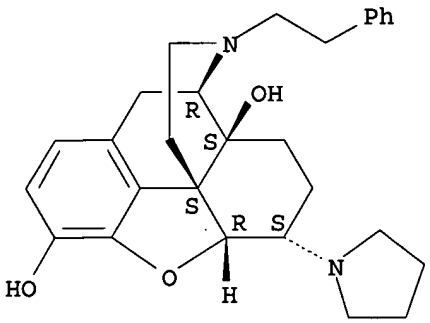
RN 13851-14-4 CAPLUS
CN Morphinan-3-ol, 4,5α-epoxy-17-methyl-6α-piperidino- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13851-15-5 CAPLUS
CN Morphinan-3,14-diol, 4,5α-epoxy-17-phenethyl-6α-(1-pyrrolidinyl)-, dihydrochloride (8CI) (CA INDEX NAME)

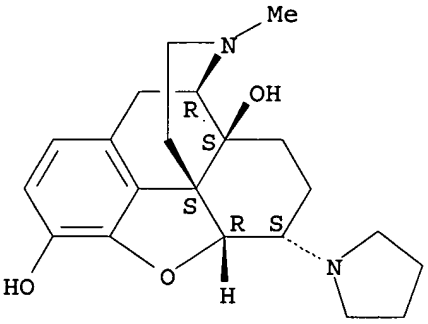
Absolute stereochemistry.



●2 HCl

RN 14912-47-1 CAPLUS
CN Morphinan-3,14-diol, 4,5α-epoxy-17-methyl-6α-(1-pyrrolidinyl)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:18786 CAPLUS
DOCUMENT NUMBER: 66:18786
TITLE: 6-Aminodihydrocorsides
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku
PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 6 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41018823	B4	19641031	JP	19640203

GI For diagram(s), see printed CA Issue.
AB I is treated with ZH, and the resulting II is reduced to give III, useful as an analgesic and antitussive. In an example, dihydrocodeinone (29.95 g.) in 300 cc. C6H6 is boiled 1.5 hrs. with 3 g. p-MeC6H4SO3H and 25 cc. pyrrolidine to give 30.2 g. II (Z = pyrrolidinyl, R1 = H, R2 = Me) (IIa), m. 155-6°. Similarly prepared are the following II (Z, R1, R2, and

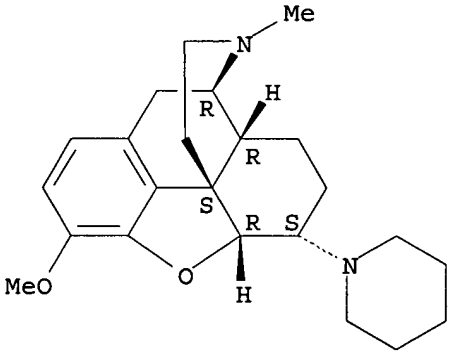
m.p. given): morpholino, H, Me, 176-8° (EtOH); 1-pyrrolidinyl, OH, Me, 189-92°; 1-pyrrolidinyl, OH, phenethyl, 176.5-8.5°; morpholino, OH, Me, 196-8°; NMe2, H, Me, 122.5-3.5° (Et2O). IIa (4.0 g.) is heated with 0.55 cc. HCO2H and the mixture dissolved in dilute HCl (pH 5.0), heated 30 min. with 0.9 g. NH2OH.HCl, made alkaline with NH4OH, and extracted with Et2O to give 0.7 g. III (X = β-(1-pyrrolidinyl), R1 = H, R2 = Me), m. 116-17° [picrate m. 237° (decomposition)], and 2.05 g. I [Z = α-(1-pyrrolidinyl), R1 = H, R2 = Me], m. 76-80°; picrate m. 245° (decomposition). Similarly prepared are the following III (Z, R1, R2, and m.p. given): α-piperidino, H, Me,-(sirupy); α-morpholino, H, Me, 138-40°; α-(1-pyrrolidinyl), OH, Me, 197-9°; α-(1-pyrrolidinyl), OH, phenethyl, 91-3°; α-morpholino, OH, Me, 184-5°; α-piperidino, OH, Me, 177-9°; α-NMe2, OH, Me, 115.5-16.5°; α-NMe2, H, Me, 96-8°.

IT **14058-51-6P 14058-76-5P 14058-77-6P 14058-80-1P 14129-39-6P 14154-70-2P 14241-46-4P 14978-25-7P 15012-13-2P 15012-14-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 14058-51-6 CAPLUS

CN Morphinan, 4,5α-epoxy-3-methoxy-17-methyl-6α-piperidino-, dihydrochloride (8CI) (CA INDEX NAME)

Absolute stereochemistry.

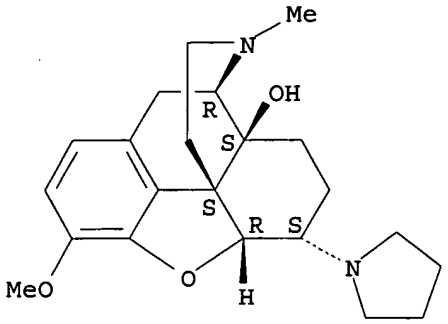


●2 HCl

RN 14058-76-5 CAPLUS

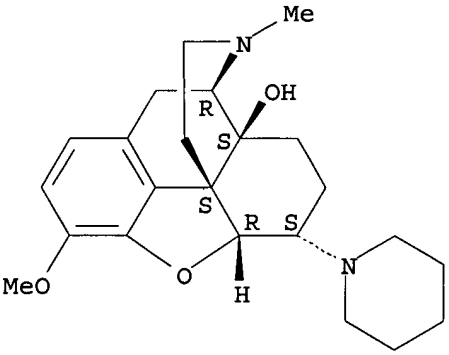
CN Morphinan, 4,5α-epoxy-3-methoxy-17-methyl-6α-(1-pyrrolidinyl)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 15012-14-3 CAPLUS
CN Morphinan-14-ol, 4,5α-epoxy-3-methoxy-17-methyl-6α-piperidino- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



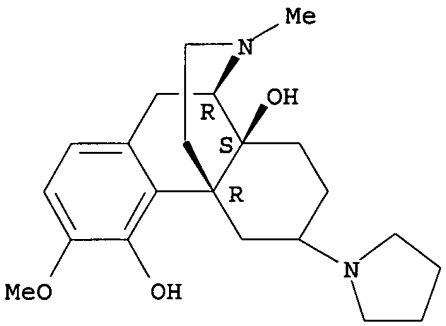
L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1966:447926 CAPLUS
DOCUMENT NUMBER: 65:47926
ORIGINAL REFERENCE NO.: 65:8980a-b
TITLE: 6-Amino-4-hydroxymorphinan derivatives
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku
PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41007787	B4	19660425	JP	19640203

PRIORITY APPLN. INFO.: JP 19640203
GI For diagram(s), see printed CA Issue.
AB cf. preceding abstract Manufacture of the same compds. as in the preceding abstract by the catalytic reduction of I in the presence of R1H (R1 = 1-pyrrolidinyl, morpholino, piperidino, or NMe2) was described.
IT **6681-21-6**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)-
(preparation of)
RN 6681-21-6 CAPLUS

CN Morphinan-4,14-diol, 3-methoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

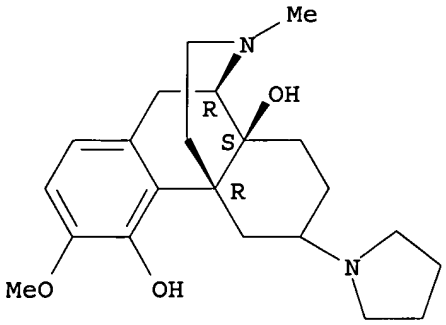


L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1966:447925 CAPLUS
DOCUMENT NUMBER: 65:47925
ORIGINAL REFERENCE NO.: 65:8979f-h,8980a
TITLE: 6-Amino-4-hydroxymorphinan derivatives
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku
PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41007786	B4	19660425	JP	19640203

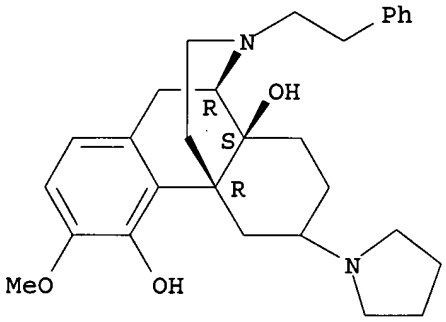
PRIORITY APPLN. INFO.: JP 19640203
GI For diagram(s), see printed CA Issue.
AB cf. following abstract Manufacture of I, useful as an analgesic and antitussive, by the catalytic reduction of II was described. In an example, 3.52 g. (--)-II (R1 = 1-pyrrolidinyl, R2 = H, R3 = Me) is dissolved in 160 cc. MeOH, shaken in a H stream at room temperature with 1 g. 10% Pd-C 3 hrs., filtered, the filtrate evaporated in vacuo, the residue dissolved in 30 cc. C6H6, passed through a column of 40 g. Al2O3, and eluted with 1: 1 C6H6-Et2O to give 2.9 g. (--)-I (R1 = 1-pyrrolidinyl, R2 = H, R3 = Me), m. 165.5-7.5°, [α]D28.5-17.4° (CHCl3). Similarly prepared are the following (--)-I (R1, R2, R3, and m.p. given): morpholino, H, Me, 226.5-8.5° piperidino, H, Me, 172-4°; piperidino, OH, Me, 113-15° (dipicrate m. 210-12° NMe2, H, Me, - (dipicrate m. 235°); NMe2, OH, Me, 171-4° 1-pyrrolidinyl, OH, phenethyl, - (dihydrochloride m. 275-80°).
IT **6681-21-6**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)- **6681-27-2**, Morphinan, 4,14-dihydroxy-3-methoxy-N-phenethyl-6-(1-pyrrolidinyl)-, dihydrochloride, (-)- (preparation of)
RN 6681-21-6 CAPLUS
CN Morphinan-4,14-diol, 3-methoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6681-27-2 CAPLUS
CN Morphinan, 4,14-dihydroxy-3-methoxy-N-phenethyl-6-(1-pyrrolidinyl)-, dihydrochloride, (-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1966:438671 CAPLUS
DOCUMENT NUMBER: 65:38671
ORIGINAL REFERENCE NO.: 65:7229h,7230a-b
TITLE: 6-Amino-substituted morphinan derivatives
INVENTOR(S): Iwai, Issei; Minakami, Akihiko; Seki, Isao; Takagi, Hiroshi; Kobayashi, Shinsaku
PATENT ASSIGNEE(S): Sankyo Co., Ltd.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 41006905	B4	19660419	JP	19640203
PRIORITY APPLN. INFO.:			JP	19640203

GI For diagram(s), see printed CA Issue.
AB Manufacture of I, useful as an analgesic and an antitussive, was described. E.g., to a solution of 3.3 g. 14-hydroxydihydrothebainone 4-methyl ether in 60 cc. MeOH are added 1.0 cc. pyrrolidine and 0.5% 10% Pd-C, the whole is shaken 8 hrs. in a H stream, filtered, and the filtrate evaporated to give 2.6 g. I (R1 = Me, R2 = OH, R3 = 1-pyrrolidinyl), m. 128.5-30.5°

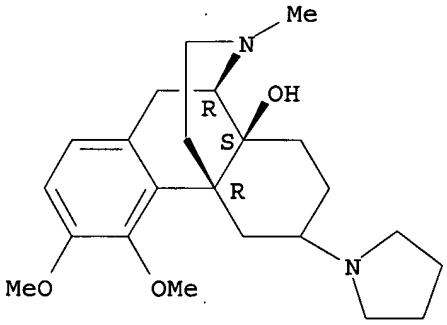
(EtOH), [α]29D -15.1° (CHCl3). Similarly prepared are the following I (R1, R2, R3, m.p., and [α]D/temperature in CHCl3 given): H, H, 1-pyrrolidinyl, 166-8°, -17.4°/28.5°; Me, H, 1-pyrrolidinyl, 81-3°, -10.5°/27.5°; H, H, 1-pyrrolidinyl, 120-1° (dipicrate m. 183-4°), -13.2°/28°; H, OH, morpholino, 183-5°, -4.1°/28.5°; H, H, NMe2, - (dipicrate m. 235°), -; H, H, NMe2, 171-4°, -; H, H, piperidino, 172-4°, -21.1°/28°. Also prepared are (-)-4,14-dihydroxy-3-methoxy-N-phenethyl-6-(1-pyrrolidinyl)morphinan, syrupy; di-HCl salt m. 275-80° (decomposition).

IT **6681-19-2**, Morphinan, 14-hydroxy-3,4-dimethoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)- **6681-20-5**, Morphinan, 3,4-dimethoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)- **6681-21-6**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)- **6681-22-7**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-morpholino-, (-)- **6681-27-2**, Morphinan, 4,14-dihydroxy-3-methoxy-N-phenethyl-6-(1-pyrrolidinyl)-, dihydrochloride, (-)- **6691-48-1**, Morphinan, 4-hydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, (-)- **6691-49-2**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, dipicrate, (-)-
(preparation of)

RN 6681-19-2 CAPLUS

CN Morphinan-14-ol, 3,4-dimethoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

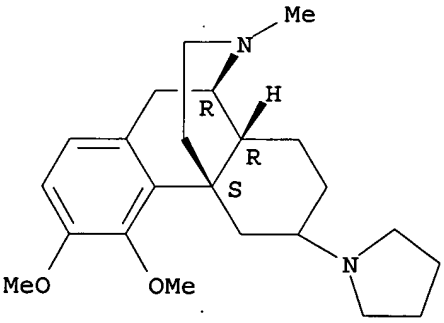
Absolute stereochemistry.



RN 6681-20-5 CAPLUS

CN Morphinan, 3,4-dimethoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

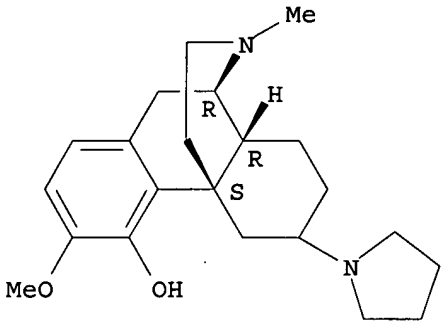
Absolute stereochemistry.



RN 6681-21-6 CAPLUS

RN 6691-48-1 CAPLUS
CN Morphinan, 4-hydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)- (7CI, 8CI) (CA INDEX NAME)

Absolute stereochemistry.

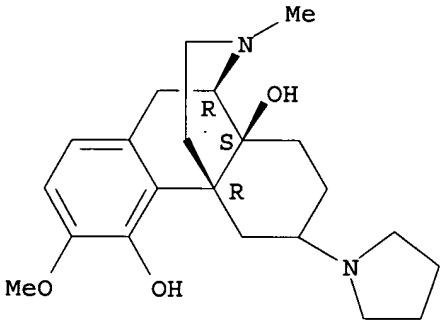


RN 6691-49-2 CAPLUS
CN Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, dipicrate (7CI, 8CI) (CA INDEX NAME)

CM 1

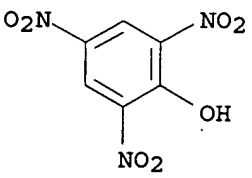
CRN 6681-21-6
CMF C22 H32 N2 O3

Absolute stereochemistry.



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



L4 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

10/530,664

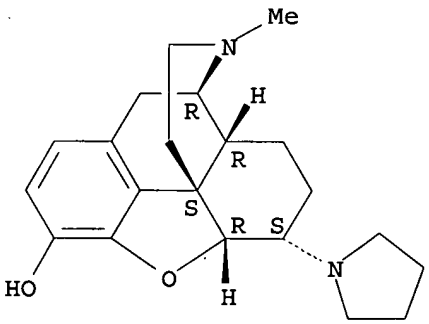
ACCESSION NUMBER: 1964:454991 CAPLUS
DOCUMENT NUMBER: 61:54991
ORIGINAL REFERENCE NO.: 61:9545f-h
TITLE: Morpholine alkaloids. XI. Aminomorphide compounds. 3. The steric aspects of the amino group
AUTHOR(S): Seki, Isao
CORPORATE SOURCE: Sankyo Co., Ltd., Tokyo
SOURCE: Yagugaku Zasshi (1964), 84(7), 631-7
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Codeine 6α-O-p-toluenesulfonate (4.5 g.) is refluxed with 20 ml. pyrrolidine in 200 ml. C6H6 for 36 hrs. to give 2.6 g. 6β-(1-pyrrolidinyl)codide (I), [α]27D --168.6° (EtOH); dipicrate m. 258-60°. I (3 g.) dissolved in 50 ml. 10% AcOH is shaken under H with 1 g. 5% Pd-C for 7 hrs. to give 1.3 g. 6β-(1-pyrrolidinyl)dihydrocodide, m. 113-16°. Starting from the corresponding 14-hydroxy derivative, 6α-(1-pyrrolidinyl)-14-hydroxycodide [m. 104-8°, [α]27D --169° (EtOH)], and 6α-(1-pyrrolidinyl)-14-hydroxydihydrocodide (m. 193-5°) were prepared The use of piperidine instead of pyrrolidine gave 6α-piperidino-14-hydroxydihydrocodide, m. 170-3° (EtOH). The preparation of 8β-piperidinotetrahydrodeoxycodeine [m. 181-3°, [α]27D -- 11.4° (CHCl3)] by reduction of 8β-piperidinodihydrocodeinone was also reported. The nuclear magnetic resonance spectra of these compds. were discussed.

IT **13851-12-2**, Morphine, 6-deoxy-7,8-dihydro-6-(1-pyrrolidinyl)- **13851-13-3**, Morphine, 6-deoxy-7,8-dihydro-6β-piperidino- **13851-14-4**, Morphine, 6-deoxy-7,8-dihydro-6α-piperidino- **14241-46-4**, Codeine, 6-deoxy-7,8-dihydro-6β-(1-pyrrolidinyl)- **14912-47-1**, Morphine, 6-deoxy-7,8-dihydro-14-hydroxy-6-(1-pyrrolidinyl)- **15012-13-2**, Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6α-(1-pyrrolidinyl)- **15012-14-3**, Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6α-piperidino- **106972-60-5**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6α-(1-pyrrolidinyl)- (preparation of)

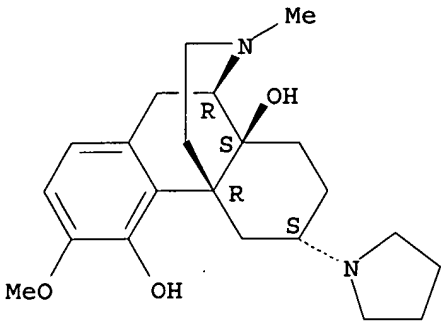
RN 13851-12-2 CAPLUS
CN Morphinan-3-ol, 4,5-epoxy-17-methyl-6-(1-pyrrolidinyl)-, (5α,6α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13851-13-3 CAPLUS
CN Morphinan-3-ol, 4,5-epoxy-17-methyl-6-(1-piperidinyl)-, (5α,6β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

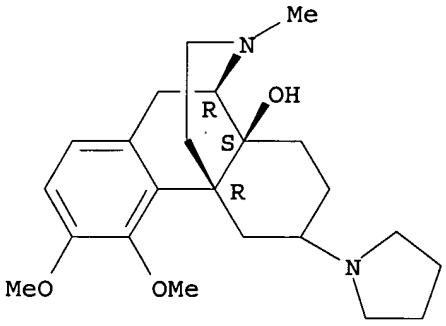


L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:454990 CAPLUS
DOCUMENT NUMBER: 61:54990
ORIGINAL REFERENCE NO.: 61:9545c-f
TITLE: Morpholine alkaloids. X. Aminomorpholide compounds. 2. The reduction of enamines and the catalytic reductive amination of C-6 ketones
AUTHOR(S): Seki, Isao
CORPORATE SOURCE: Sankyo Co., Ltd., Tokyo
SOURCE: Yagugaku Zasshi (1964), 84(7), 626-31
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Enamine (I) (0.005 mole) dissolved in 150 ml. MeOH is stirred at 35-40° with 0.5 g. $NaBH_4$ for 2 hrs. and then refluxed with 1 ml. AcOH for 3 hrs. to give the following II [R1, R2, R3, m.p., and [α]D ($CHCl_3$) given]: H, Me, α-pyrrolidino, 70-80°, -237.8°; H, Me, β-pyrrolidino, 116-17°, -152.6°; H, Me, piperidino, --, --; H, Me, morpholino, 138-40°, -156.8°; OH, Me, pyrrolidino, 197-9°, -160.4°; OH, phenethyl, pyrrolidino, 91-3°, -85°; OH, Me, piperidino, 177-9°, -170°; OH, Me, morpholino, 184-5°, -162.9°; H, Me, NMe_2, 96-8°, -155.2°; OH, Me, NMe_2, 115.5-16.5°, -158.1°. Reduction of I with HCO_2H also gives II. Preparation of III by the catalytic (Pd-C) reductive amination of the corresponding C-6 ketone in MeOH is also described. The following III are prepared [R1, R2, R3, m.p., and [α]D ($CHCl_3$) given]: H, H, pyrrolidino, 165.5-7.5°, -17.4°; H, Me, pyrrolidino, 81-3°, -10.5°; OH, H, piperidino, -- (dipicrate m. 210-12°), --; H, H, morpholino, 226.5-8.5°, 5.2°; H, H, piperidino, 172-4°, -21.1°; OH, H, morpholino, 183-5°, 4.1°; OH, H, pyrrolidino, 120.5-1.5° (dipicrate m. 183-6°), -13.2°; OH, Me, pyrrolidino, 128.5-30.5°, -15.1°; H, H, NMe_2, -- (dipicrate m. 235°), --; OH, H, NMe_2, 172-5°, --. The preparation of the following compds. was also reported: (-)-N-phenethyl-3-methoxy-6-(1-pyrrolidinyl)-4,14-dihydroxymorphinan (dihydrochloride m. 275-80°), 6-(1-pyrrolidinyl)dihydromorphide (m. 130-5°), 6-(1-pyrrolidinyl)-14-hydroxydihydromorphide (m. 254-6°), 6-piperidinodihydromorphide (α-form m. 213-16°, β-form m. 216.5-17.5°), and 6-dimethylamino-14-hydroxydihydromorphide (m. 261-4°).
IT **6681-19-2**, Morphinan, 14-hydroxy-3,4-dimethoxy-N-methyl-6-(1-pyrrolidinyl)- **6681-20-5**, Morphinan, 3,4-dimethoxy-N-methyl-6-(1-pyrrolidinyl)- **6681-21-6**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)- **6681-22-7**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-morpholino- **6681-26-1**, Morphinan, 4-hydroxy-3-methoxy-N-methyl-6-piperidino- **6681-27-2**,

Morphinan, 4,14-dihydroxy-3-methoxy-N-phenethyl-6-(1-pyrrolidinyl)-, dihydrochloride **6691-48-1**, Morphinan, 4-hydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)- **6691-49-2**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-(1-pyrrolidinyl)-, dipicrate **7315-45-9**, Morphinan, 4-hydroxy-3-methoxy-N-methyl-6-morpholino- **7315-46-0**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-piperidino- **7315-47-1**, Morphinan, 4,14-dihydroxy-3-methoxy-N-methyl-6-piperidino-, dipicrate **13851-12-2**, Morphine, 6-deoxy-7,8-dihydro-6-(1-pyrrolidinyl)- **13851-13-3**, Morphine, 6-deoxy-7,8-dihydro-6β-piperidino- **13851-14-4**, Morphine, 6-deoxy-7,8-dihydro-6α-piperidino- **13851-21-3**, Norcodeine, 6-deoxy-7,8-dihydro-14-hydroxy-N-phenethyl-6-(1-pyrrolidinyl)- **14058-51-6**, Codeine, 6-deoxy-7,8-dihydro-6-piperidino-, dihydrochloride **14058-76-5**, Codeine, 6-deoxy-7,8-dihydro-6α-(1-pyrrolidinyl)- **14058-77-6**, Codeine, 6-deoxy-7,8-dihydro-6-morpholino- **14058-80-1**, Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6-morpholino- **14154-70-2**, Codeine, 6-deoxy-7,8-dihydro-6α-(1-pyrrolidinyl)-, dipicrate **14241-46-4**, Codeine, 6-deoxy-7,8-dihydro-6β-(1-pyrrolidinyl)- **104195-72-4**, Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6-piperidino- **107305-16-8**, Codeine, 6-deoxy-7,8-dihydro-6β-(1-pyrrolidinyl)-, dipicrate **834885-34-6**, Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6-(1-pyrrolidinyl)-
(preparation of)

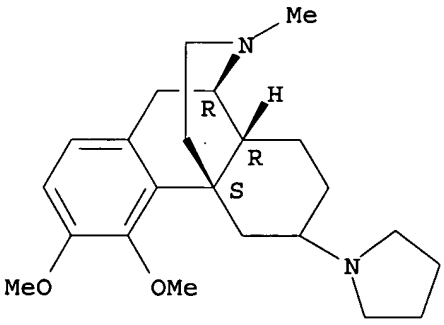
RN 6681-19-2 CAPLUS
CN Morphinan-14-ol, 3,4-dimethoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



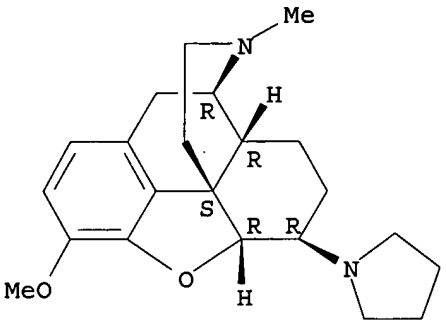
RN 6681-20-5 CAPLUS
CN Morphinan, 3,4-dimethoxy-17-methyl-6-(1-pyrrolidinyl)-, (-)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



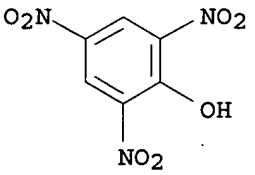
CMF C22 H30 N2 O2

Absolute stereochemistry.



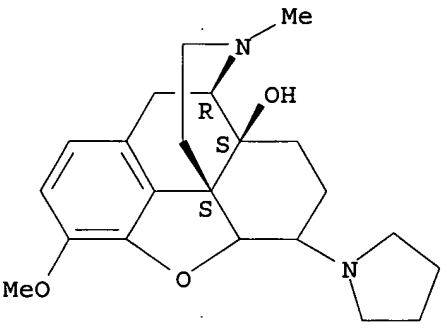
CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



RN 834885-34-6 CAPLUS
CN Codeine, 6-deoxy-7,8-dihydro-14-hydroxy-6-(1-pyrrolidinyl)- (7CI) (CA INDEX NAME)

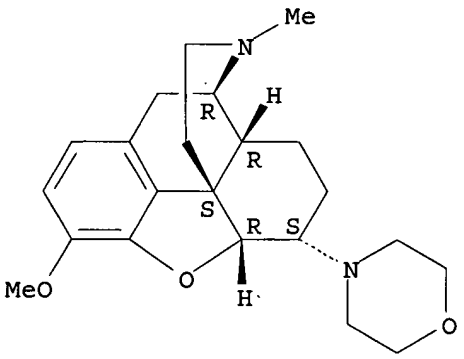
Absolute stereochemistry.



L4 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:454989 CAPLUS
DOCUMENT NUMBER: 61:54989
ORIGINAL REFERENCE NO.: 61:9544h,9545a-c
TITLE: Morpholine alkaloids. IX. Aminomorphide compounds. 1. The formation of enamines and the addition of amine to α,β-unsaturated ketones
AUTHOR(S): Seki, Isao
CORPORATE SOURCE: Sankyo Co., Ltd., Tokyo

SOURCE: Yagugaku Zasshi (1964), 84(7), 621-5
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB I (0.01 mole) dissolved in 70 ml. C6H6 is boiled with 0.02 mole secondary amine and 0.03 g. p-MeC6H4SO3H to give the following II [X, R1, R2, R3,% yield, m.p., and [α]D (CHCl3) given]: H, H, Me, pyrrolidino, 85.6, 155.5-6.5°, -352.5°; H, OH, Me, pyrrolidino, 94.7, 189-92°, --320.7; H, OH, phenethyl, pyrrolidino, 98.2, 176.5-8.5°, -220.7°; H, OH, H, pyrrolidino, 66.7, 210-12° (decomposition), --; pyrrolidino, OH, Me, pyrrolidino, 94.25, 166°, -38.8°; H, H, Me, morpholino, 81.7, 176-8°, -321.6°; H, OH, Me, morpholino, 86.5, 196-8°, -294.8°; H, H, Me, Me2N, 50, 122.5-3.5°, -285.7°; Me2N, OH, Me, Me2N, 32, 148-51°, -236.5°. III (0.01 mole) is refluxed with 0.01 mole secondary amine in C6H6 for 1.5-2 hrs. to give the following IV [R1, R2, % yield, m.p., and [α]D (CHCl3) given]: H, piperidino, 39.7, 186-7°, -75.5°;H, morpholino, 33.5, 203, --78.2°; OH, pyrrolidino, --, 165-6°, -151.1°; OH, piperidino, --, 174-6°, -158.3°; OH, morpholino, --, 206.5-8.5°, -178.8°; OH, NMe2, --, 174-5°, -187.1°.
IT **14058-77-6**, Codeine, 6-deoxy-7,8-dihydro-6-morpholino- (preparation of)
RN 14058-77-6 CAPLUS
CN Morphinan, 4,5α-epoxy-3-methoxy-17-methyl-6α-morpholino- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1939:54200 CAPLUS
DOCUMENT NUMBER: 33:54200
ORIGINAL REFERENCE NO.: 33:7800e-i,7801a-e
TITLE: Aminomorphides and aminocodides
AUTHOR(S): Small, Lyndon; Palmer, Fred S.
SOURCE: Journal of the American Chemical Society (1939), 61, 2186-90
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB There are today no distinctive phys. or chemical criteria that may be applied to the determination of the configuration of groups at C-6 or C-8 relative to any arbitrarily chosen standard. Certain derivs. have been classified as having the codeine or isocodeine, the pseudocodeine or allopseudocodeine

configuration on the basis of similarities in pharmacol. action, with full realization of the limitations and weakness of such deductions. Positional differences between the unsatd. 6- and 8-substituted types may be determined by catalytic reduction; those derivs. having the substituent (or H) in the 8-position and a double bond at the 6,7-position on reduction suffer an opening of the O bridge simultaneously with or before saturation of the double bond. The derivs. with the 6-substituent (halogen excepted) and the 7,8-double bond undergo hydrogenation normally, without involving the O bridge. The reaction of α-chloromorphide (I) and α-chlorocodide (II) with secondary amines or NH3 proceeds with a rearrangement such that the new basic groups appear at the 8-position. The morphine derivs. that are believed to have the halogen atom in the 8-position, as bromomorphide (III), bromocodide (IV) and β-chlorocodide (V), react with a rearrangement in the reverse sense, to give 6-aminomorphide and 6-aminocodide derivs. The introduction of basic groups into the morphine or codeine mol. results in a considerable diminution of physiol. action, especially analgesic effect. I and Et2NH give 8-diethylaminomorphide (VI), m. 201-4° [α]D21 49.1° (MeOH, c 0.87) (cf. Wieland and Kappelmeier, C. A. 5, 3462); the di-HI derivative, with 1.5 moles of H2O, m. 87-93°, [α]D25 2.6° (H2O, c 0.38); diperchlorate, m. 114-16°, [α]D19 4.4° (H2O, c 0.91). Heating 10 g. I and piperidine in an evacuated sealed tube at 100° for 30 min. gives 9.2 g. of 8-piperidinomorphide (VII), m. 222-4°, [α]D24 28.7° (MeOH, c 1.15); di-HI salt, m. 208-14°, [α]D23 14.9° 14.9° (H2O, c 0.37); monomethiodide, m. 243-5°, [α]2D2323.7° (50% EtOH, c 1.14); catalytic reduction yields a tetrahydro derivative, m. 270-80°, [α]D26 45.1° (10% AcOH, c 0.63); FeCl3 gives a moss-green color; Ac2O gives a base, m. 172-8°. 8-Diethylaminocodide, resulting from II and Et2NH or from VI and CH2N2, m. 101-3°, [α]D23 42.6° (MeOH, c 1); diperchlorate, m. 180.5-3°, [α]D19 3.3° (H2O, c 0.92); di-HI salt, m. 179- 82°, [α]D2622.9° (EtOH, c 0.39); tetrahydro derivative, m. 154-7°, [α]D25 31.5° (MeOH), c 0.75); monoperchlorate, m. 234-8°, [α]D26 18.3° (H2O, c 0.30). 8-Piperidocodide (VIII), from II and piperidine or from VII and CH2N2, m. 116-17°, [α]D22 25.8° (MeOH, c 0.89); di-H sulfate, with 2 moles of H2O, m. 161-3.5°, [α]D26 19.8° (H2O, c 1.46); mono-HI salt, m. 234-7°, [α]D24 13.3° (H2O, c 0.337); most prepns. of the HI salt consisted chiefly of the di-HI salt; monomethiodide, [α]D25 22° (H2O, c 0.86); diperchlorate, m. 181-3°, [α]D25 13.2° (50% EtOH, c 1.02); tetrahydro derivative (IX), m. about 125°, [α]D25 36.7° (MeOH, c 1.07); the FeCl3 reaction is deep emerald-green. The HCl salt of VIII (from VIII and HCl in Et2O) on reduction yields a dihydro derivative of VIII, m. 167-9°, [α]D25 -1.2° (MeOH, c 1.68), and some IX. II (10 g.) in 180 cc. liquid NH3, kept at 50° for 24 hrs., gives 11 g. of the di-HCl salt (X), m. 300-5°, [α]D24 -40.7° (H2O, c 0.88), of 8-aminocodide (XI), m. 128.5-9°, [α]D21 -79.2° (EtOH, c 0.48); di-Ac derivative, m. 218-20° (decomposition), [α]D24 -83.1° (EtOH), c 1.04); tetrahydro derivative, m. 138.5-40°, [α]D24 -9.7° (EtOH, c 1.13); FeCl3 gives an intense blue-green color; di-HCl salt, [α]D24 6.6° (H2O, c 0.91); reduction of X gives a glassy dihydro derivative of XI, [α]D21 -28.70° (EtOH, c 1.08); di-HCl salt, m. 274-7°, [α]D24 -14.7° (H2O, c 1.08). III (20 g.) and 20 g. piperidine, heated in a sealed evacuated tube for 30 min. in a boiling water bath, give 14.6 g. of 6-piperidomorphide (XII), m. 216-17°, [α]D23 -234.8° (MeOH, c 0.871); methiodide, m. 236-41°, [α]D23 -145.8° (50% EtOH, c 1.05); dihydro derivative, m. 215-17°, [α]D24 -155.9° (MeOH, c 0.76). IV or V and piperidine or XII and CH2N2 give 6-piperidocodide, m. 75-80°, [α]D25 -233.9° (MeOH, c 0.87); diperchlorate,

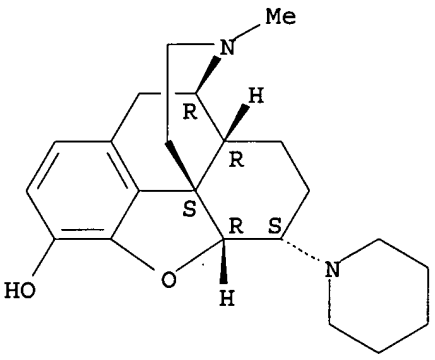
m. 172-5°, [α]D23 -113.4° (H2O, c 0.44); a crystalline reduction product could not be isolated. IV and liquid NH3 do not give a Br-free compound

IT **13851-14-4**, Morphide, dihydro-6-piperido- (preparation of)

RN 13851-14-4 CAPLUS

CN Morphinan-3-ol, 4,5α-epoxy-17-methyl-6α-piperidino- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'REGISTRY' ENTERED AT 09:02:01 ON 01 JUN 2006

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L3 376 S L1 FULL

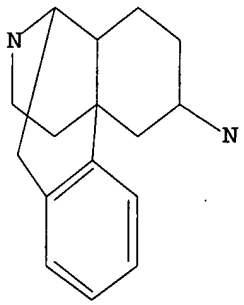
FILE 'CAPLUS' ENTERED AT 09:02:34 ON 01 JUN 2006

L4 22 S L3

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:333718 CAPLUS
DOCUMENT NUMBER: 140:339518
TITLE: Preparation of morphinan derivatives having nitrogen-containing heterocyclic group as remedies or prophylactic agents for **urinary frequency** or **urinary incontinence**
INVENTOR(S): Izumimoto, Naoki; Kawai, Koji; Kawamura, Kuniaki; Fujimura, Morihiro; Komagata, Toshikazu
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033457	A1	20040422	WO 2003-JP12890	20031008
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501389	AA	20040422	CA 2003-2501389	20031008
AU 2003272944	A1	20040504	AU 2003-272944	20031008
EP 1555266	A1	20050720	EP 2003-754030	20031008
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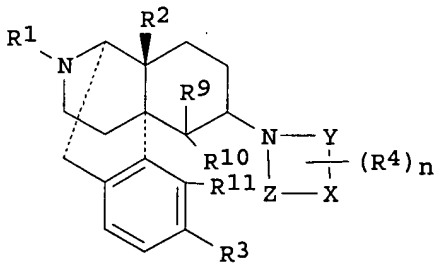
BR 2003014754	A	20050726	BR 2003-14754	20031008
US 2006040970	A1	20060223	US 2005-530664	20050406
NO 2005002167	A	20050616	NO 2005-2167	20050503

PRIORITY APPLN. INFO.:			JP 2002-295616	A 20021009
			WO 2003-JP12890	W 20031008

OTHER SOURCE(S): MARPAT 140:339518
GI



I

AB Title compds. I [wherein R1 represents Me, cyclopropylmethyl, etc.; R2 and R3 represent each hydroxy, methoxy, acetoxy, etc.; Y and Z represent each a valence bond, CO, etc.; X represents a C2-5 carbon chain constituting a

part of the cyclic structure (wherein one of the carbon atoms may be substituted by oxygen, sulfur or nitrogen); (R4)n represents an optionally substituted fused benzene ring, carbonyl, etc.; R9 represents hydrogen, etc.; R10 and R11 may be bonded together to form O; and R6 represents hydrogen, etc.] and their pharmacol. acceptable salts, useful as remedy or a prophylactic agents for **urinary frequency** or **urinary incontinence**, are prepared Thus, refluxing dihydrocodeinone with 1,2,3,4-tetrahydroquinoline in xylene-DMF in the presence of methanesulfonic acid gave, after treatment with sodium cyanohydride and methanesulfonic acid in methanol at room temperature for 24 h, 33% 4,5α-epoxy-6β-tetrahydroquinolino-3-methoxy-17-methylmorphinan (II). II was converted to 4,5α-epoxy-6β-tetrahydroquinolino-17-methylmorphinan-3-ol tartrate (III) in 75% yield. III showed urinary contraction inhibitory activity at 0.1 mg/kg i.v. in rats.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 12:57:54 ON 01 JUN 2006
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L2 376 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:58:21 ON 01 JUN 2006
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L4 1481 S URINARY FREQUENCY OR URINARY INCONTINENCE OR URINARY URGENCY
L5 1 S L3 AND L4

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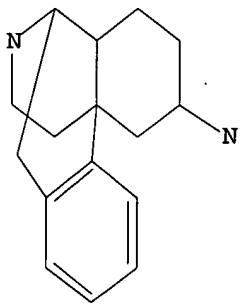
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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